

Figure 1

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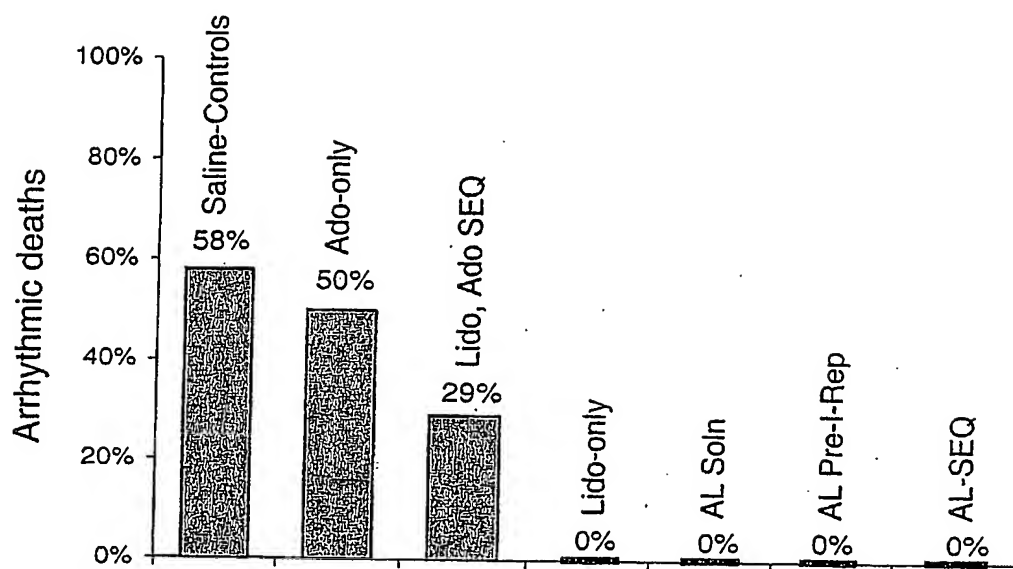


Figure 2

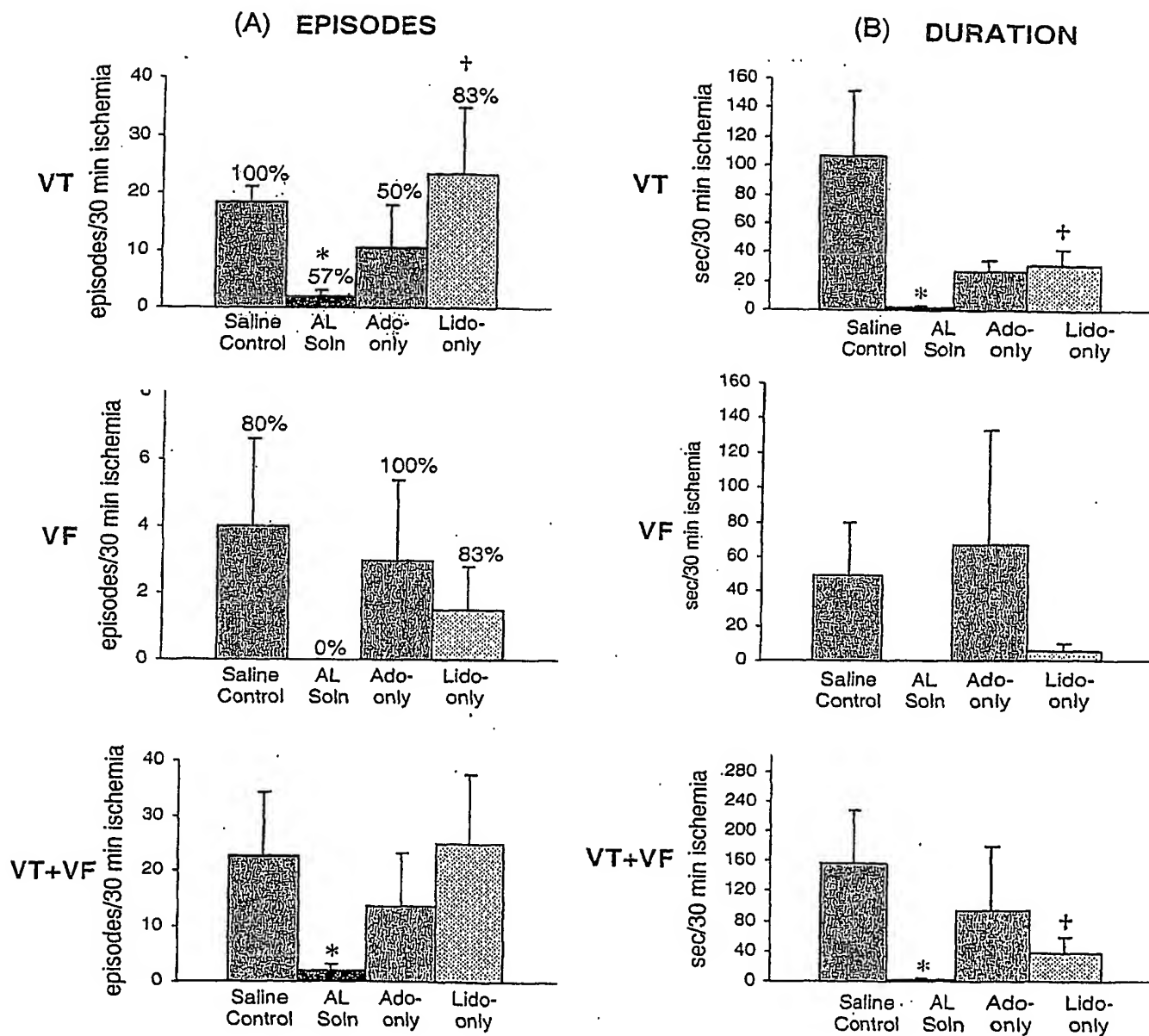


Figure 3

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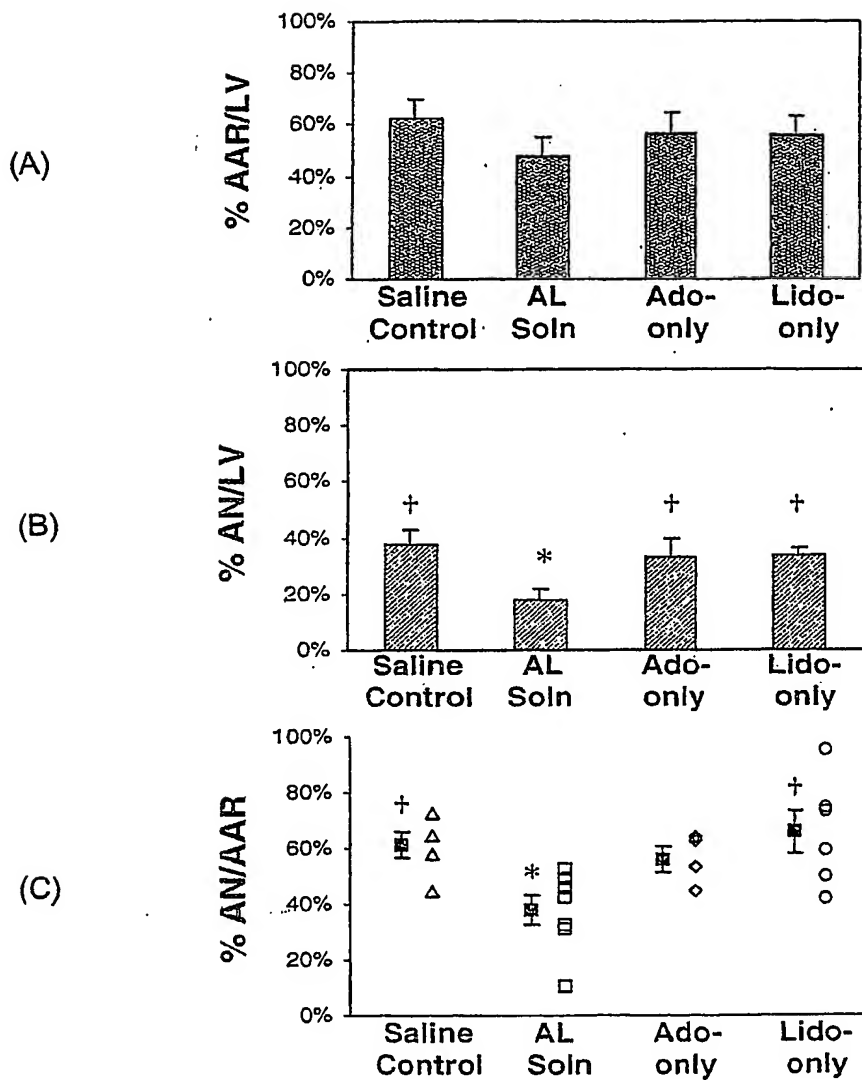


Figure 4

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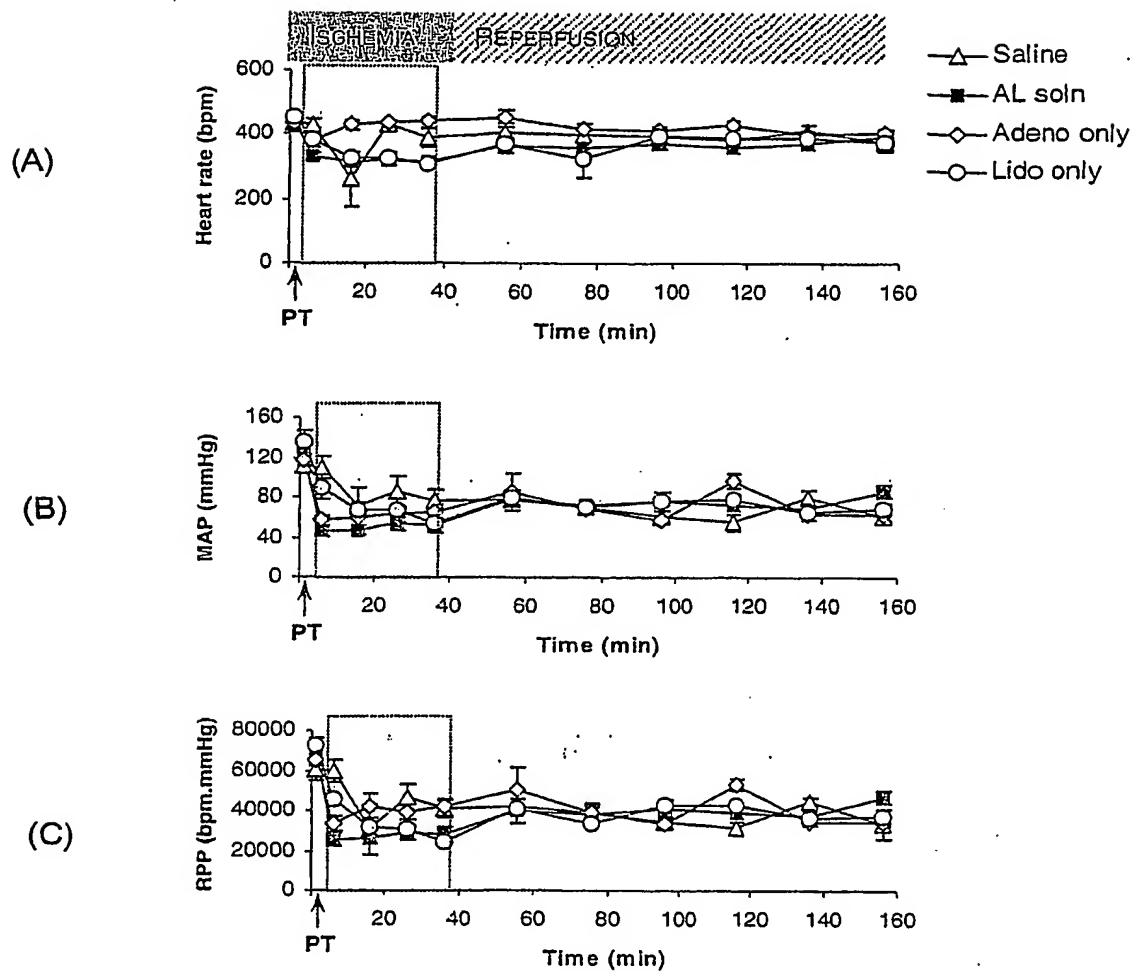


Figure 5

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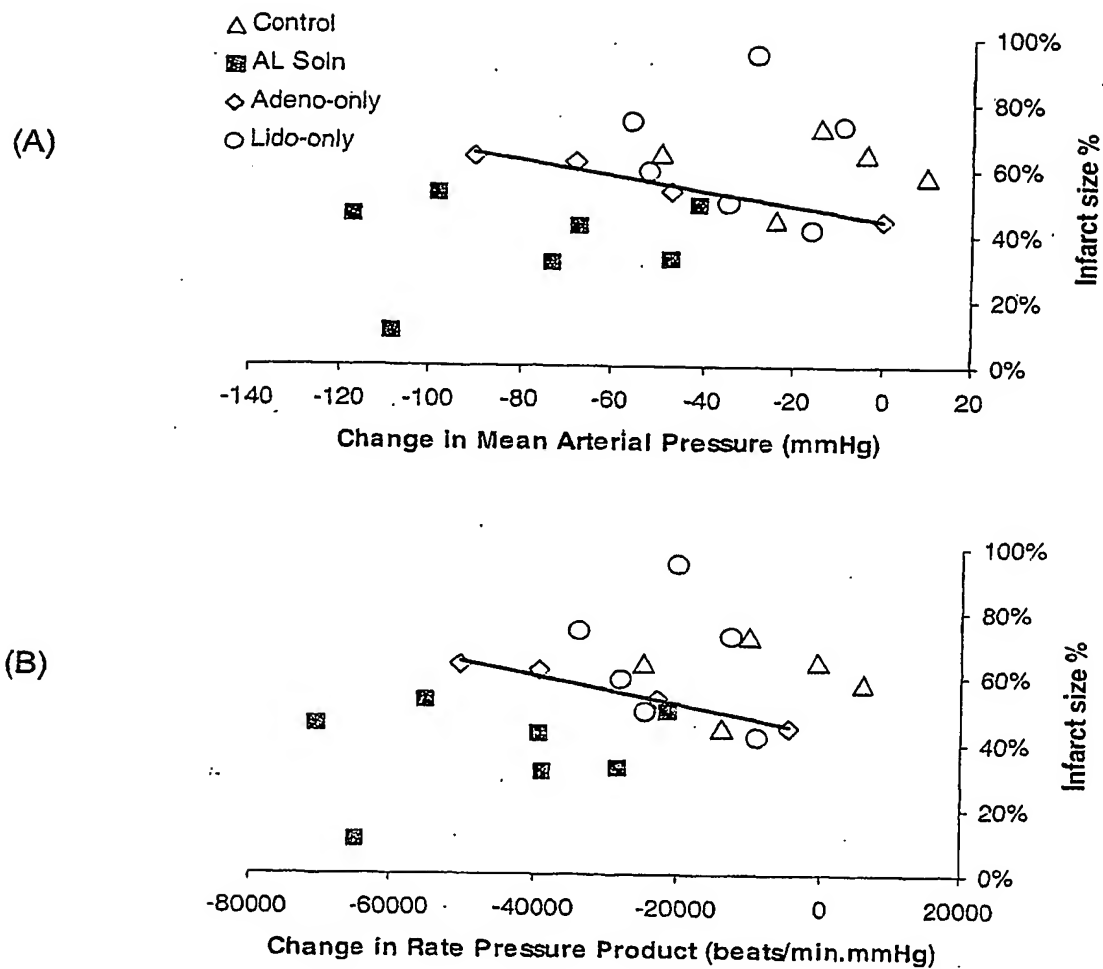


Figure 6

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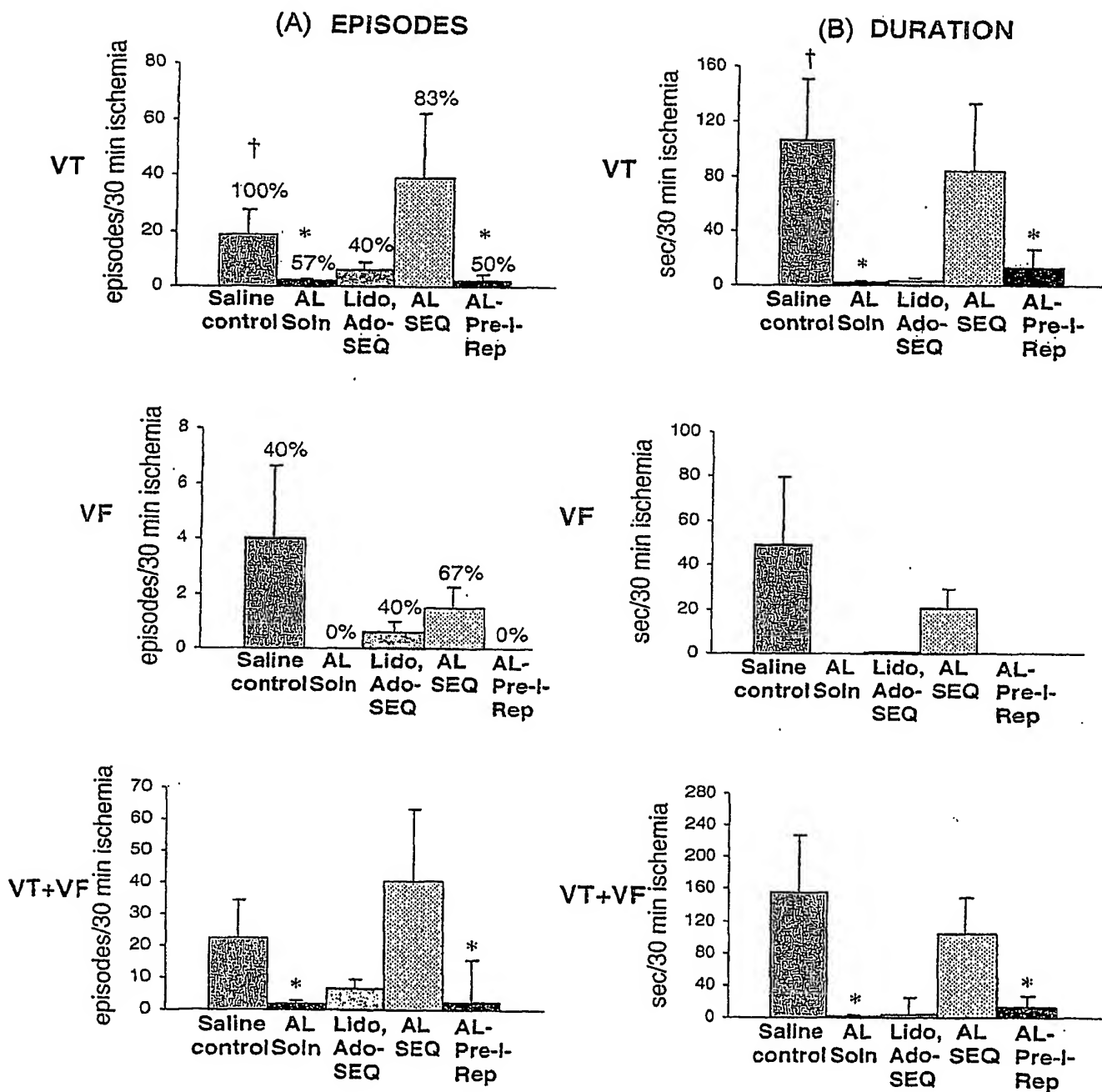


Figure 7

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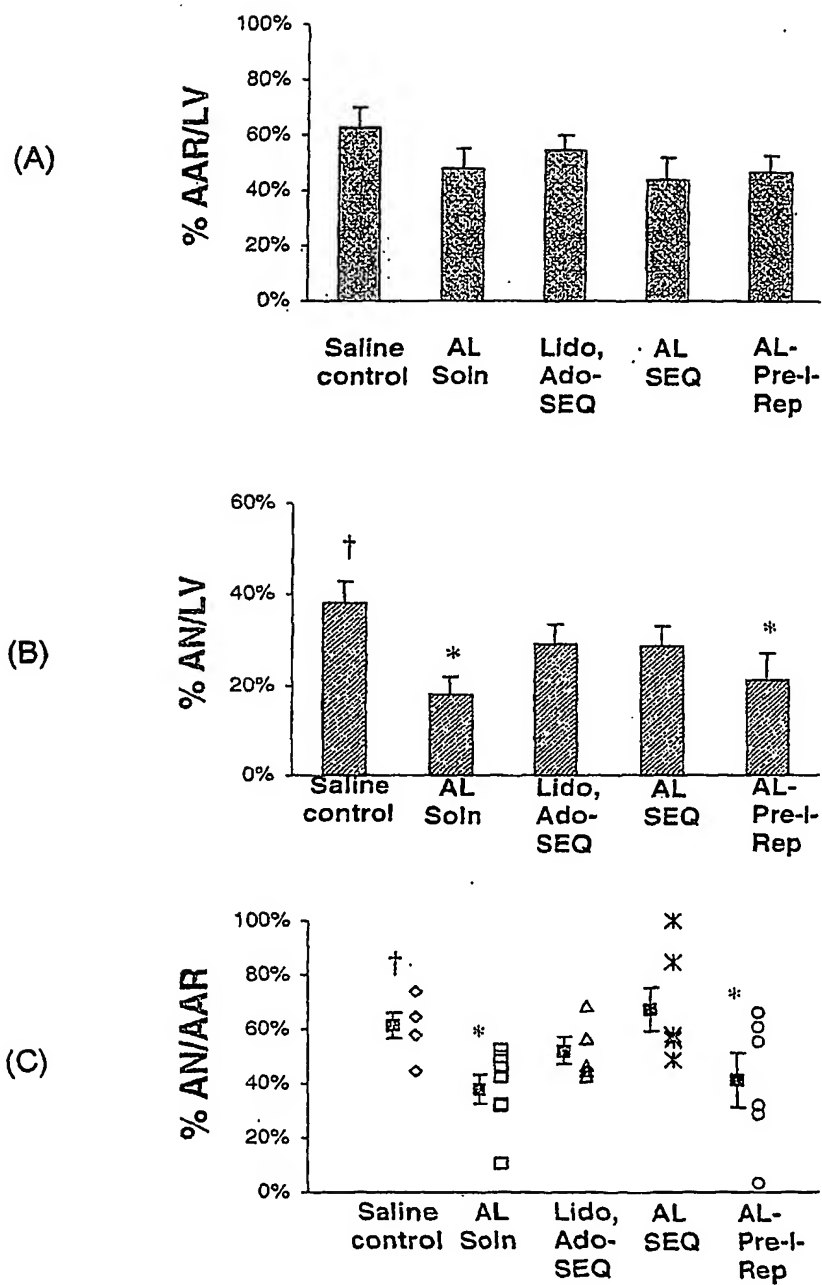


Figure 8

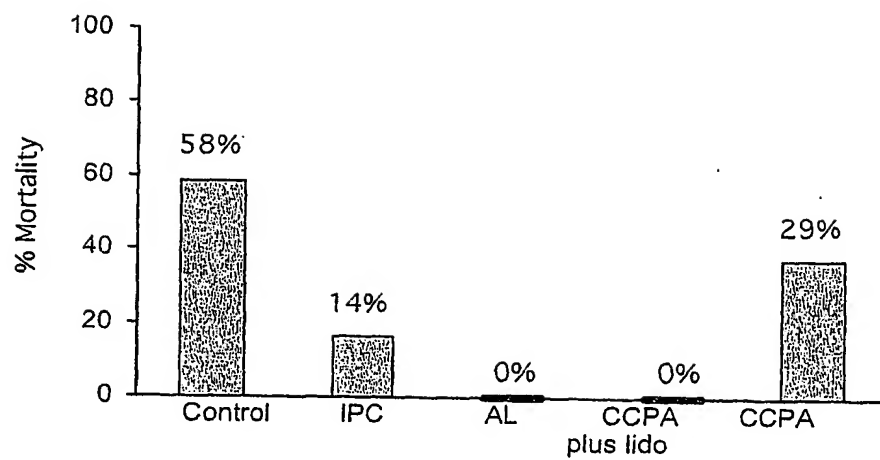


Figure 9

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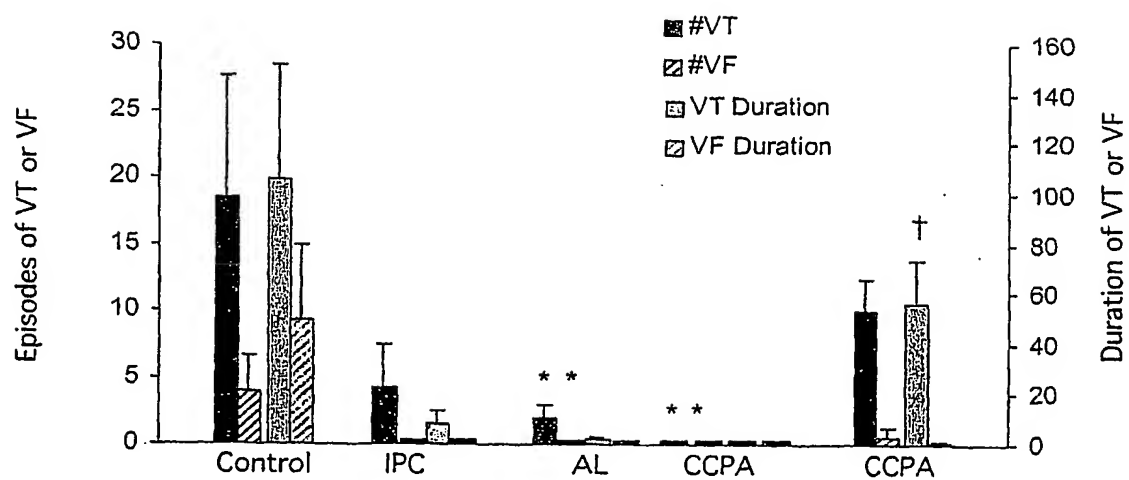


Figure 10

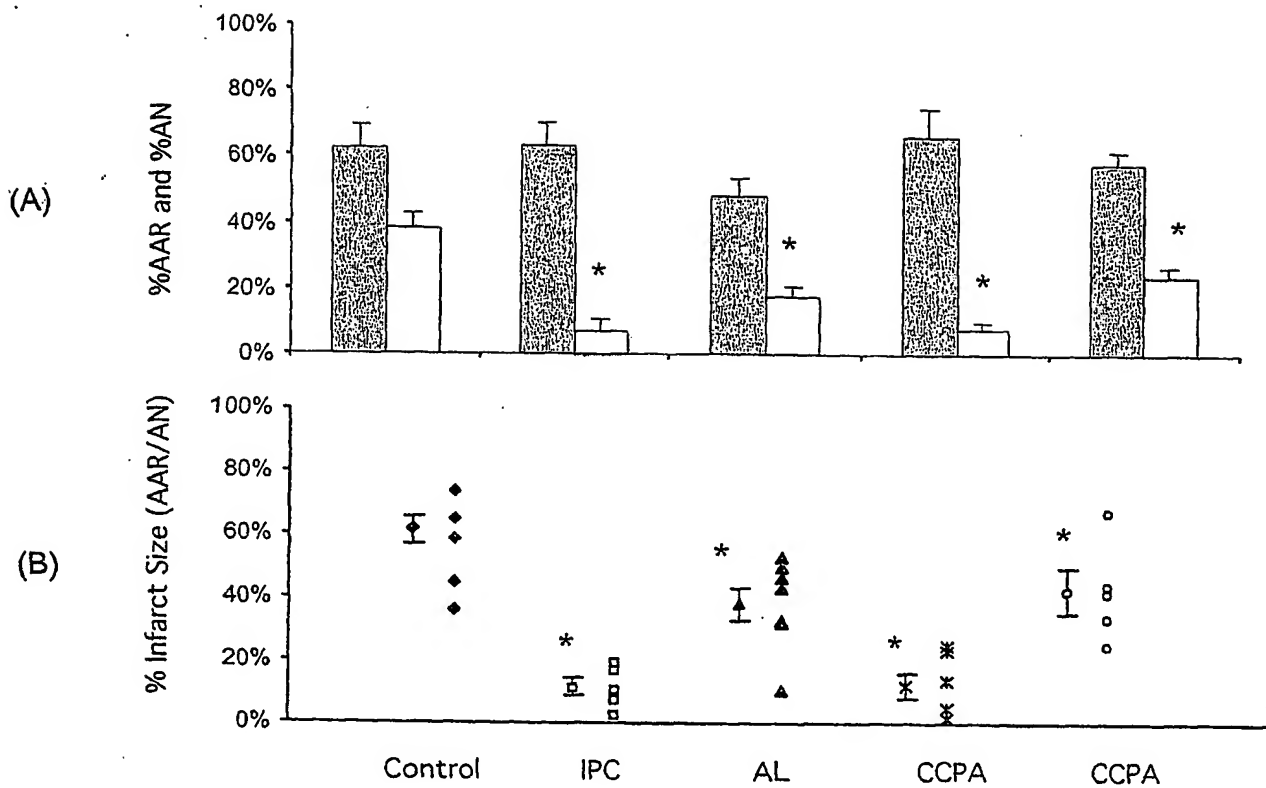


Figure 11

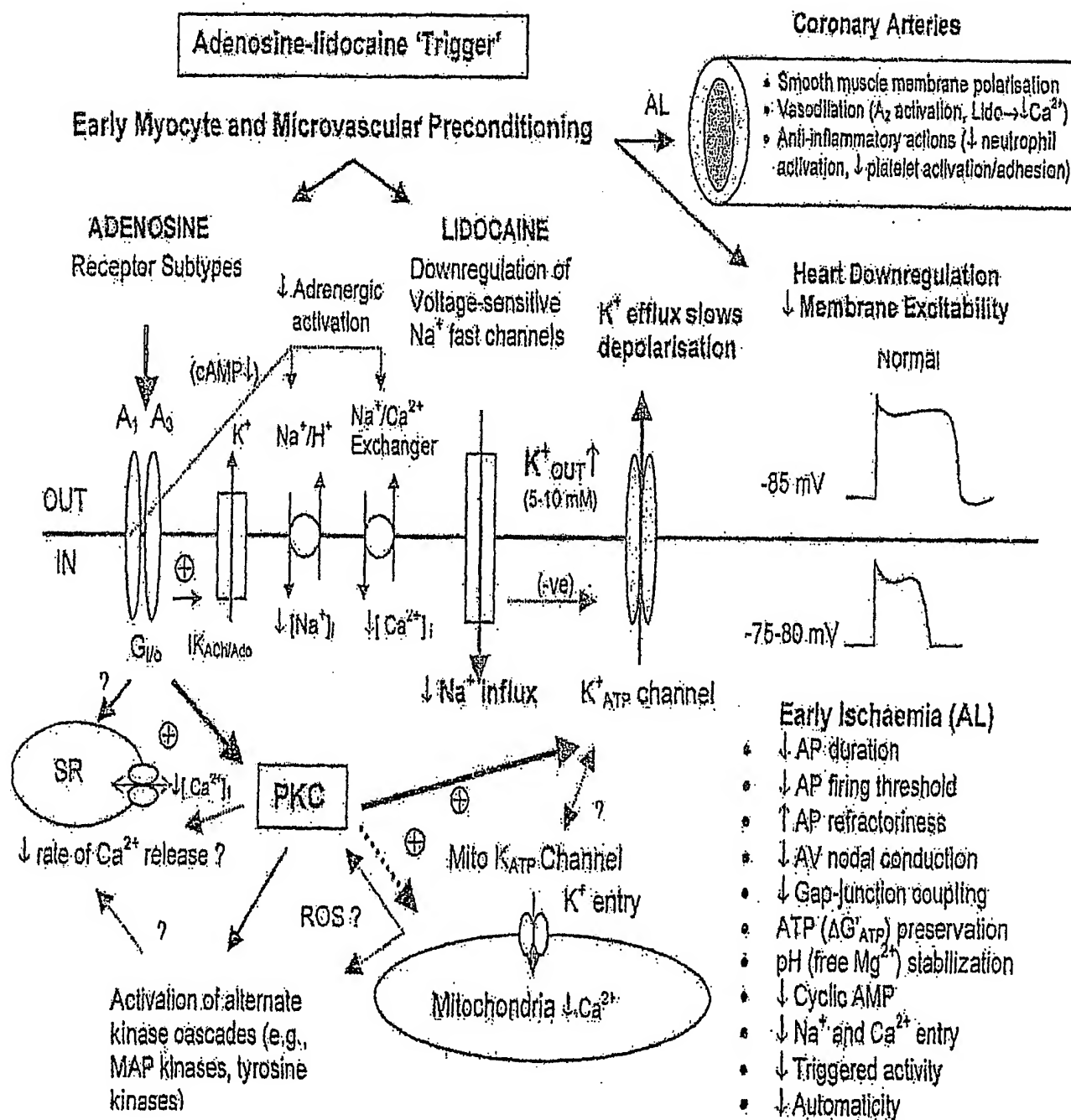


Figure 12

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Table 2:

30 min Arrest Protocol	n	Time to Arrest (sec)	Cardioplegia flow (ml/min)	Heart Rate (bpm)	Systolic/ diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1			295	120/70	33	15.5
ARREST 5 min Induction @18 min (for 2 min) @30 min (2 min) RECOVERY		14 sec	10	ARREST	ARREST	ARREST	ARREST
			3	ARREST	ARREST	ARREST	ARREST
			4.5	ARREST	ARREST	ARREST	ARREST
15 min				225	110/70	10.5	13.5
30 min				246	110/75	12	12
45 min				223	110/78	12.5	11

Figure 13

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Table 3:

30 min Arrest Protocol	n	Time to Arrest (sec)	Cardioplegia flow (ml/min)	Heart Rate (bpm)	Systolic/diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1			244	115/65	35.5	16
ARREST 5 min		23 sec	9	ARREST	ARREST	ARREST	ARREST
Induction @18 min (for 2 min)			7	ARREST	ARREST	ARREST	ARREST
@30 min (2 min) RECOVERY			6	ARREST	ARREST	ARREST	ARREST
15 min				184	120/60	33	16.5
30 min				255	90/70	5	12
45 min				271	85/65	3	10

Figure 14

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Table 4:

30 min Arrest Protocol	n	Time to Arrest (sec)	Cardioplegia flow (ml/min)	Heart Rate (bpm)	Systolic/ diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1			206	110/70	21	10
ARREST 5 min Induction @18 min (for 2 min)		25 sec	5	ARREST	ARREST	ARREST	ARREST
@30 min (2 min) RECOVERY			4	ARREST	ARREST	ARREST	ARREST
			2.5	ARREST	ARREST	ARREST	ARREST
5 min				119	120/60	9	4
15 min				154	100/70	4	5
45 min				154	90/70	4	2

Figure 15

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Table 5:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/ diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
E-ARREST (5 min)	1		350	120/70	40	16
ARREST		1 min 45 sec	ARREST	ARREST	ARREST	ARREST
5 min Induction						
@15 min			ARREST	ARREST	ARREST	ARREST
(for 2 min)						
@30 min			ARREST	ARREST	ARREST	ARREST
(2 min)						
RECOVERY						
First Beat after reperfusion		39 min				
48 min			243	110/70	23	18
60 min			338	115/70	36	14
75 min			342 (98% return)	110/70 (>90% return)	37 (93% return)	16 (100% return)

Figure 16

Table 6:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/ diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1		298	120/80	36	13.5
ARREST		17 sec	ARREST	ARREST	ARREST	ARREST
5 min Induction						
@15 min (for 2 min)			ARREST	ARREST	ARREST	ARREST
@30 min (2 min)			ARREST	ARREST	ARREST	ARREST
RECOVERY						
First Beat after reperfusion		5 min 41 sec				
15 min			Very	Weak	0	
32 min			281	90/80	15	13
45 min			263	120/80	39	10
60 min			275	120/80	33	12
65 min			300	120/80	28.5	12
			(100% return)	(100% return)	(79% return)	(89% return)

Figure 17

Table 7:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1		247	110/70	36	12
ARREST						
5 min Induction		3 min 26 sec	ARREST	ARREST	ARREST	ARREST
@15 min (for 2 min)			ARREST	ARREST	ARREST	ARREST
@30 min (2 min)			ARREST	ARREST	ARREST	ARREST
RECOVERY						
First Beat after reperfusion		49 sec				
5 min			180	110/70	23.5	7.5
15 min (leak 5 ml/min)			223	110/90	27.5	8
30 min (leak 5 ml/min)			224 (91% return)	110/90 (>90% return)	27 (75% return)	8 (67% return)

Figure 18

Table 8:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	2		290 270	130/70 120/70	47 42	15.5 15
ARREST		17 sec	ARREST	ARREST	ARREST	ARREST
5 min Induction @15 min (for 2 min)		23 sec	ARREST	ARREST	ARREST	ARREST
@30 min (2 min)			ARREST	ARREST	ARREST	ARREST
RECOVERY						
First Beat after reperfusion		1 min 05 sec 1 min 13 sec				
5 min			200 234	160/60 120/80	41 34.5	17 17.5
15 min			200 234	130/70 120/70	28 38	12 13.5
30 min			327 242	120/70 110/60	37.5 37	15 12.5
45 min			319 234	120/70 110/60	37.5 34	14 11.5
			(86-110%)	(>90% return)	(80% return)	(77-90%)

Figure 19

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Table A:

L Only	Control	PAF	0.1 μ M	1 μ M	5 μ M	10 μ M
	3.26	20.74	14.14	14.44	15.28	19.42
	2.82	18.71	15.5	13.65	15.01	18.41

AVG	3.04	19.725	14.82	14.045	15.145	18.915
STD	0.311127	1.435427	0.961665	0.558614	0.190919	0.714178
SEM	0.22	1.015	0.68	0.395	0.135	0.505

ADO Only	Control	PAF	0.1 μ M	1 μ M	10 μ M	100 μ M
	2.82	16.78	9.78	5.94	0.13	1.76
	2.42	17.13	11.54	3.08	1.89	3.04

AVG	2.62	16.95	10.66	4.51	1.01	2.40
STD	0.28	0.25	1.24	2.02	1.24	0.91
SEM	0.20	0.18	0.88	1.43	0.88	0.64

AL	Control	PAF	1.00	2.00	3.00	4.00
	1.50	22.24	14.05	2.64	-3.30	0.97
	2.11	21.49	14.31	3.88	0.70	-3.61

AVG	1.81	21.87	14.18	3.26	-1.30	-1.32
STD	0.43	0.53	0.18	0.88	2.83	3.24
SEM	0.31	0.38	0.13	0.62	2.00	2.29

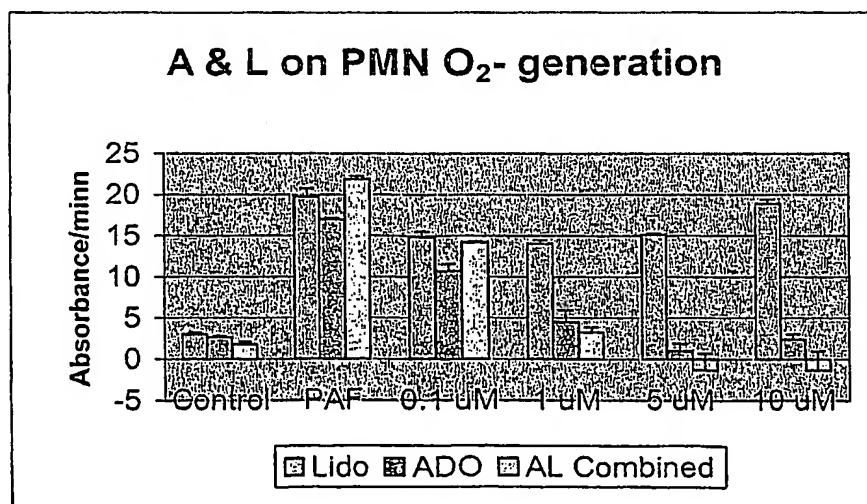


Figure 20

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Table 9:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/ diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1		360	120/80	43	18
ARREST 50 ml Induction		9 sec	ARREST	ARREST	ARREST	ARREST
@38 min (2 min) RECOVERY			ARREST	ARREST	ARREST	ARREST
First Beat after reperfusion 15 min		2 min 15 sec	320	120/70	8	11.6
30 min			335	120/70	21	11
60min			360 (100% return)	120/70 (>90% return)	23 (53% return)	11 (61% return)

Figure 21

Table 10:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1		320	120/70	39	19
ARREST 50 ml Induction		9 sec	ARREST	ARREST	ARREST	ARREST
			ARREST	ARREST	ARREST	ARREST
NO 38 min PULSE RECOVERY			ARREST	ARREST	ARREST	ARREST
First Beat after reperfusion		12 min 32 sec			Leak 2.5 ml/min	
15 min			143	120/70	6	16
30 min			264	110/75	25.5	11.5
45 min			270 (84% return)	110/80 (>90% return)	28 72% return)	10.5 (55% return)

Figure 22

Table 11:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1		350	120/70	41	15
ARREST		16 sec	ARREST	ARREST	ARREST	ARREST
50 ml Induction						
CONTINUOUS			ARREST	ARREST	ARREST	ARREST
CONTINUOUS			ARREST	ARREST	ARREST	ARREST
RECOVERY						
First Beat after reperfusion		1 min 35 sec				
15 min			280	110/70	39	13
30 min			320	120/70	38	14
60min			340 (97% return)	120/70 (>95% return)	36 (88% return)	13 (87% return)

Figure 23

Table 12:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1		300	115/80	33	20
ARREST		18 sec	ARREST	ARREST	ARREST	ARREST
50 ml Induction						
@15 min (2 min)			ARREST	ARREST	ARREST	ARREST
@38 min (2 min)			ARREST	ARREST	ARREST	ARREST
RECOVERY						
First Beat after reperfusion		2 min 52 sec				
15 min			200	115/85	8	7
30 min			220	110/70	10	7
60min			230 (77% return)	110/70 (>90% return)	7 (21% return)	7 (35% return)

Figure 24

Table 13:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1		303	140/75	34	15
ARREST		13 sec	ARREST	ARREST	ARREST	ARREST
50 ml Induction @15 min (2 min)			ARREST	ARREST	ARREST	ARREST
@28 min (2 min)			ARREST	ARREST	ARREST	ARREST
RECOVERY						
First Beat after reperfusion		4 min				
15 min		AF at 12 min	236	140/75	29.5	12.5
30 min			248	125/80	26	11.5
45min			229 (76% return)	125/80 (>90% return)	20 (59% return)	10.5 (70% return)

Figure 25

Table 14:

30 min Arrest Protocol	n	Time to Arrest and first beat (sec)	Heart Rate (bpm)	Systolic/diastolic Pressure (mmHg)	Aortic Flow (ml/min)	Coronary Flow (ml/min)
PRE-ARREST (5 min)	1		255	140/70	32	15
ARREST		8 sec	ARREST	ARREST	ARREST	ARREST
50 ml Induction @15 min (2 min)			ARREST	ARREST	ARREST	ARREST
@28 min (2 min)			ARREST	ARREST	ARREST	ARREST
RECOVERY						
First Beat after reperfusion		12 min 30 sec AF at 15 min				
15 min			204	160/70	30	22
30 min			220	140/75	21	16
45 min			229 (90% return)	140/80 (>95% return)	18 (56% return)	17 (113% return)

Figure 26

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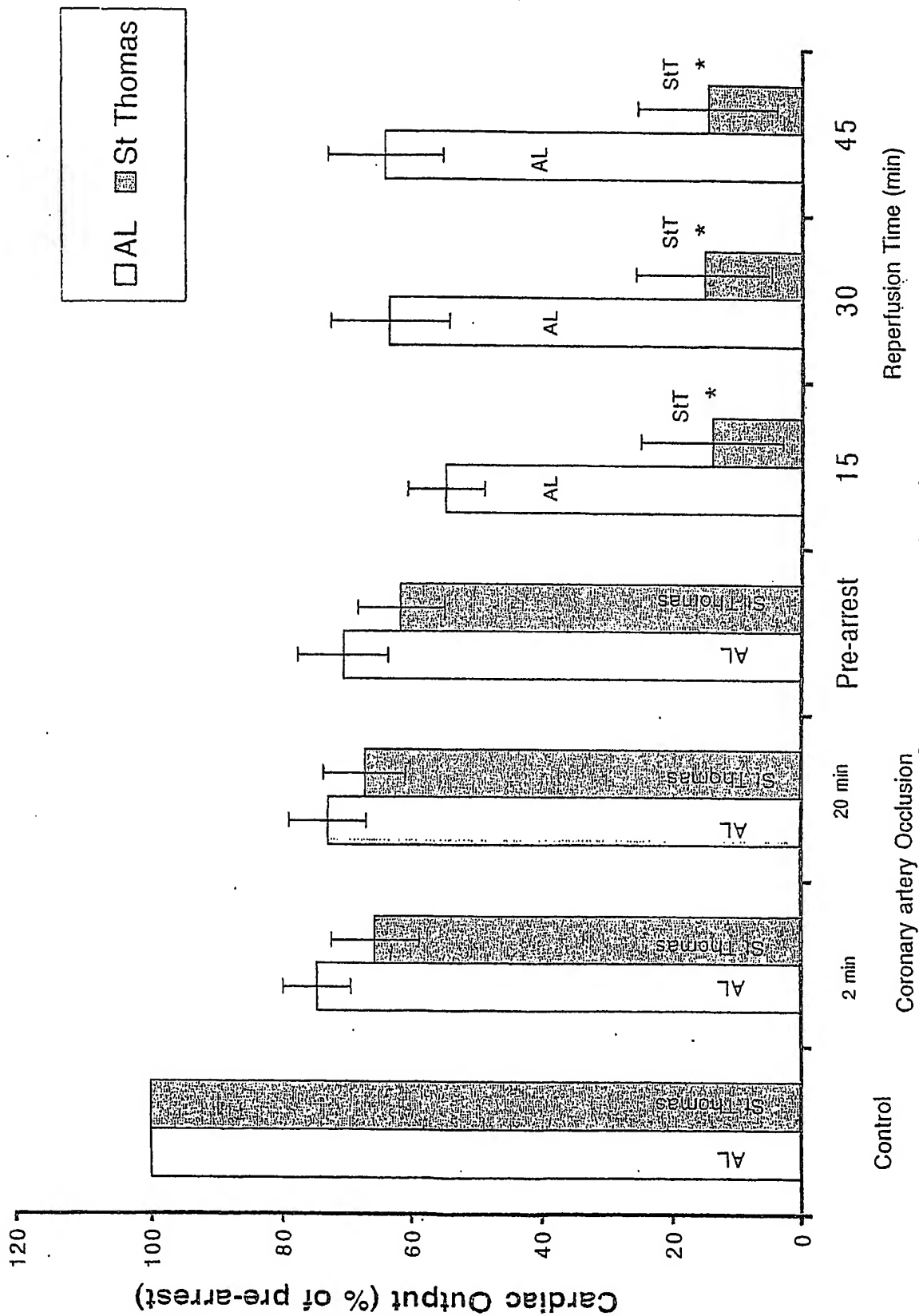


Figure 27

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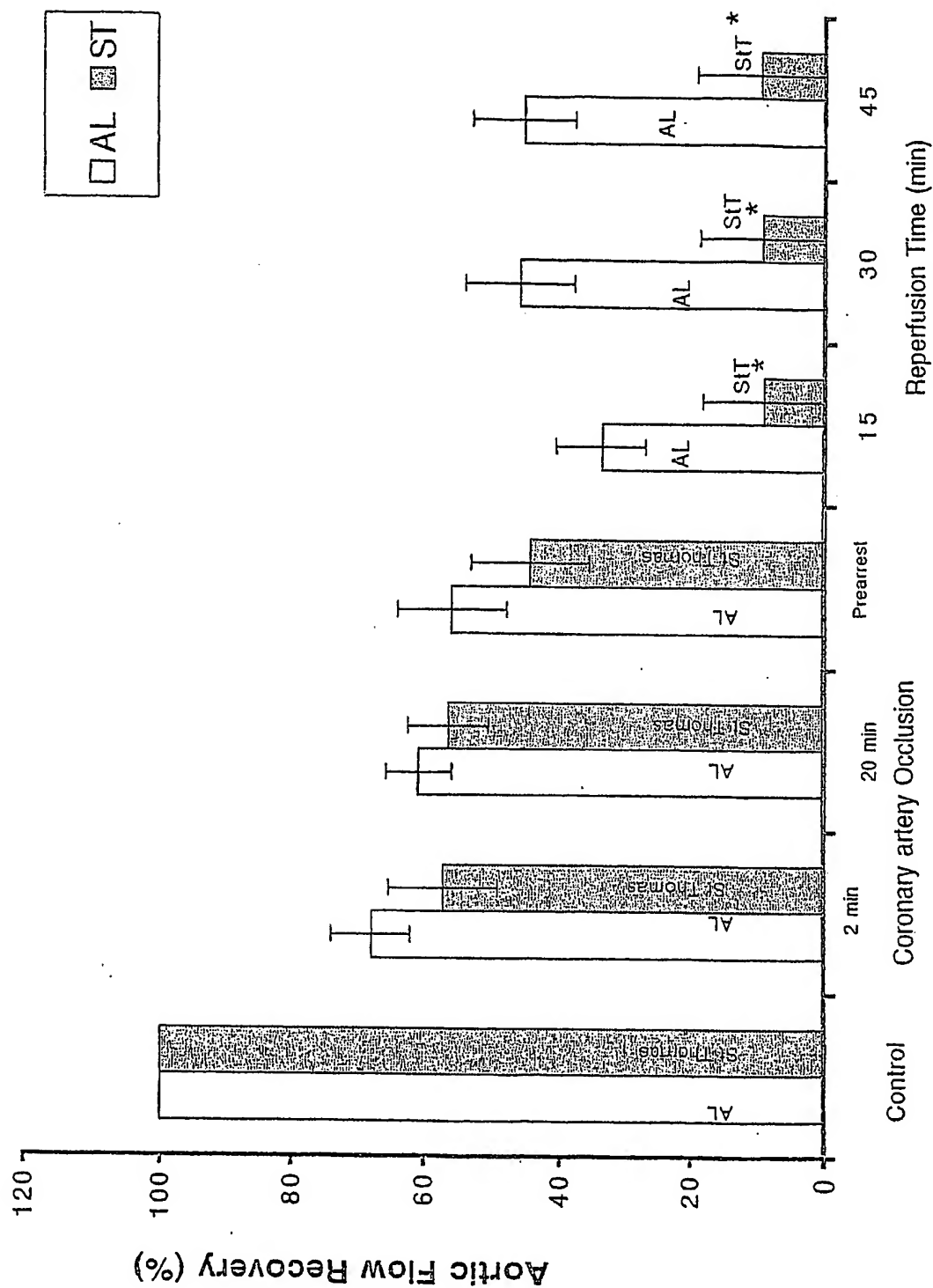


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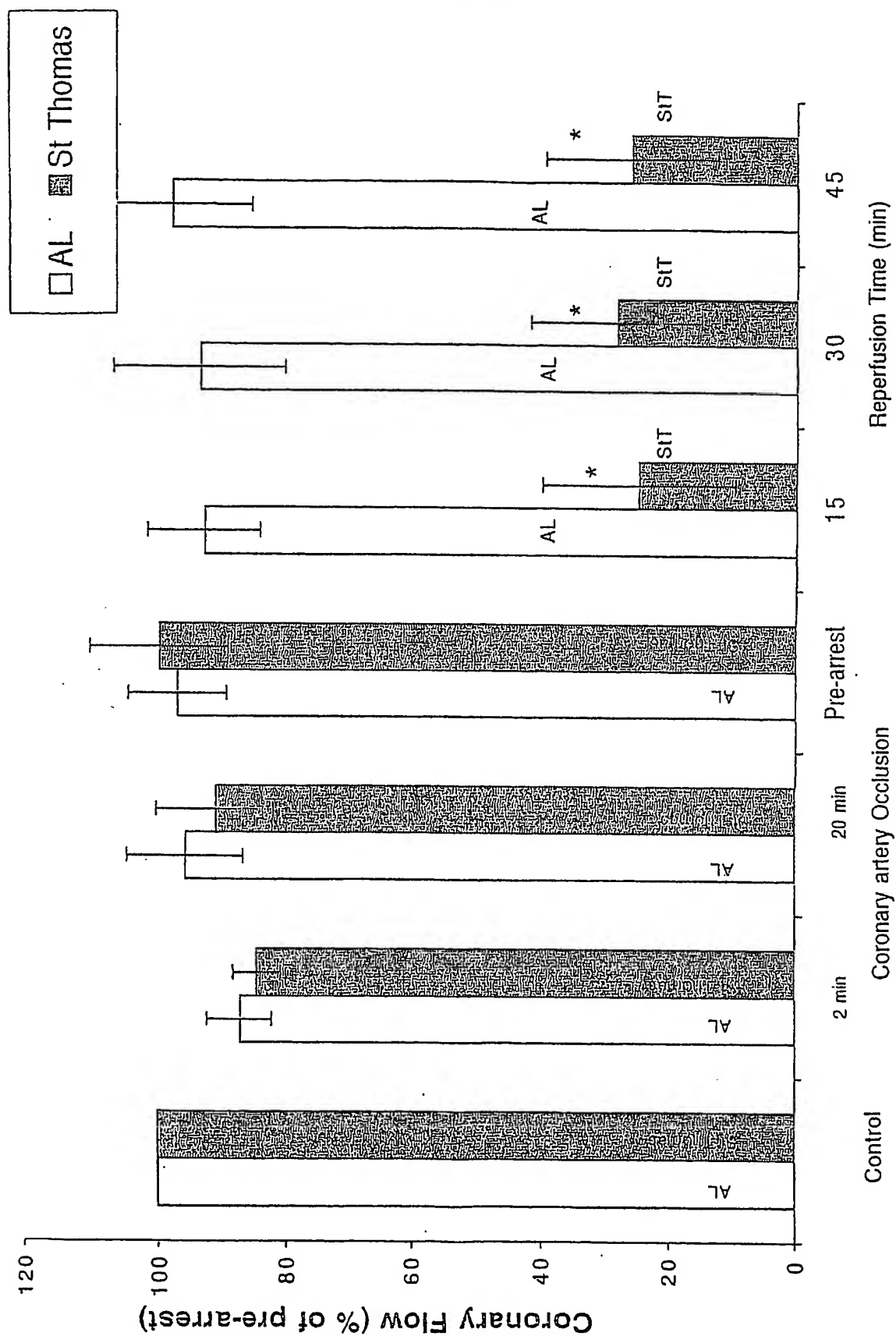


Figure 29
SUBSTITUTE SHEET (RULE 26) RO/AU

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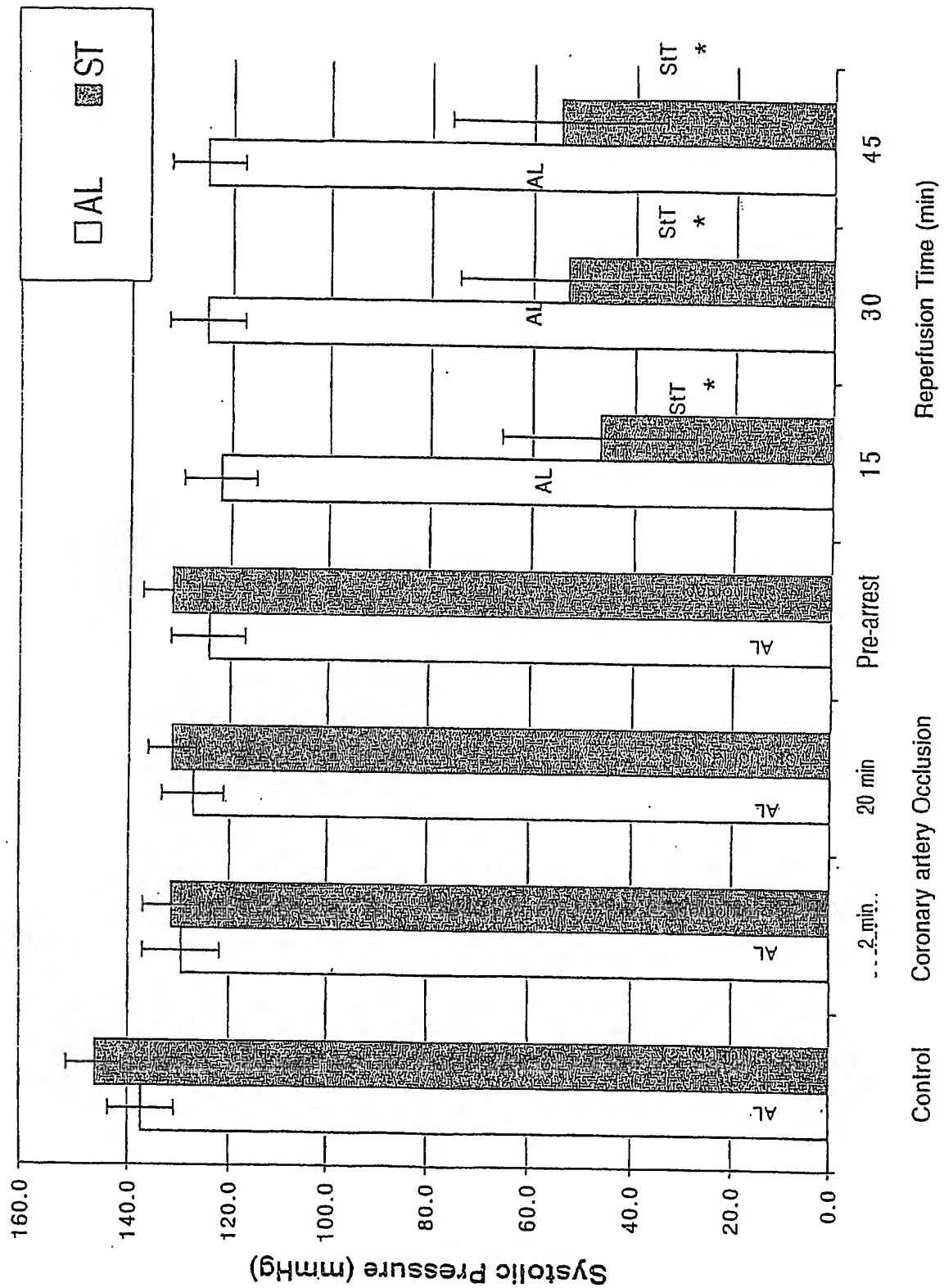


Figure 30

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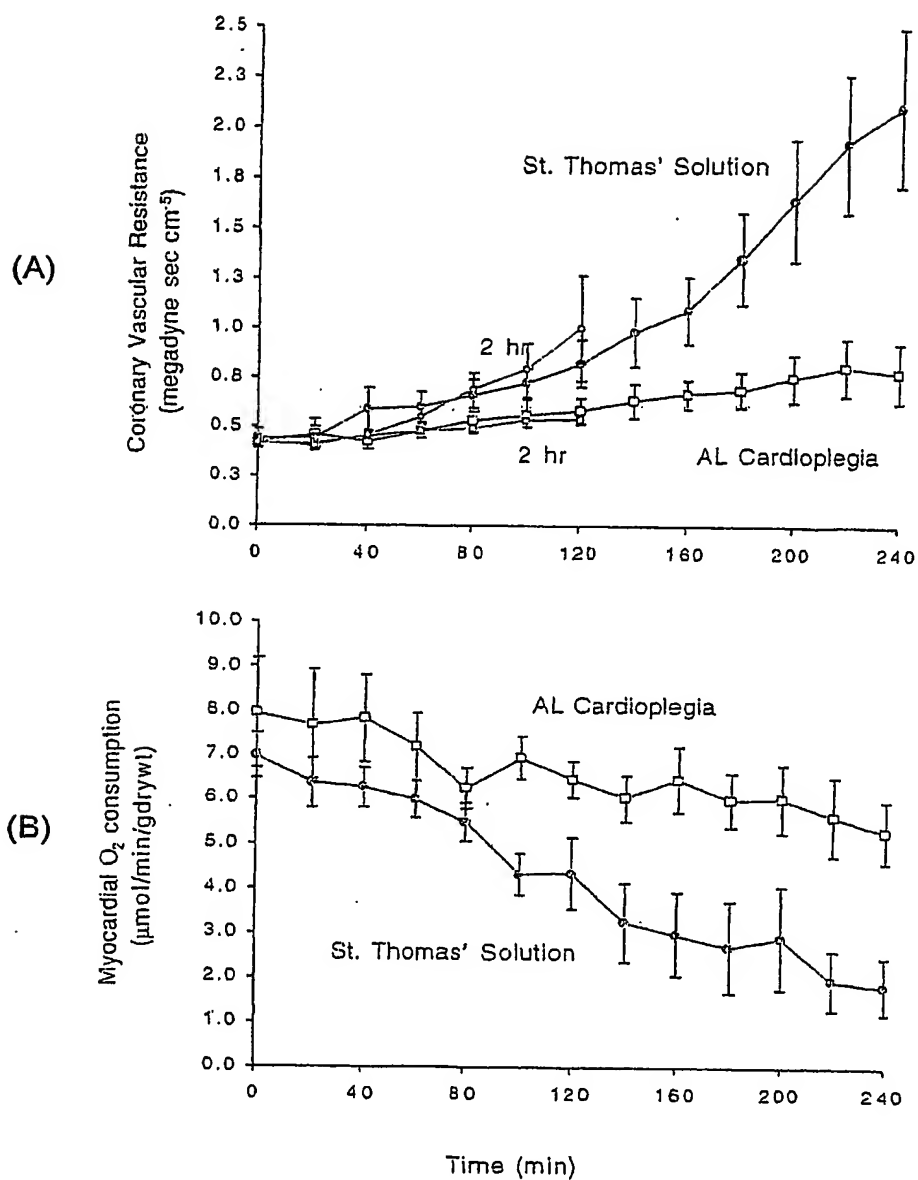


Figure 31

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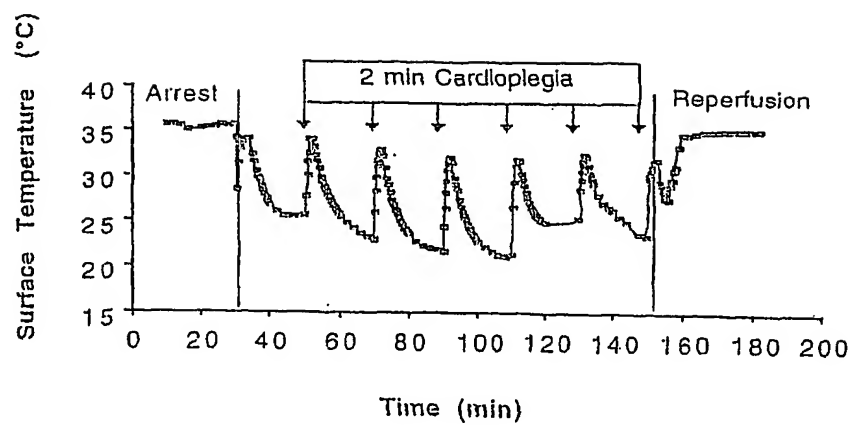


Figure 32

Table 15:

Treatment	No of hearts	Membrane potential (This study)	Published Values	References
Normal ⁵ Pre-Arrest Controls	6	-83 ± 2 mV ³	-84 ± 2 mV ²	Masuda, T, Dobson, GP and , RL (1990) J. Biol. Chem. <u>265</u> (33) 20321-34
St. Thomas Solution #2	6	-48 ± 3 mV ³	-84 ⁴ ± 1 mV ^{2, 4}	Kleber AG (1983) Circ Res. <u>52</u> (4) 442-50
16 mM KCl (8°C)	7		~ -50 mV ²	Chambers DJ (1999) Curr Opin Cardiol 14 (6) 495-500
16 mM KCl	6		-50 mV ²	Snabailis, AK, Shattock, MJ, and Chambers, DJ (1997) Circulation 96 (9) 3148-56
AL Cardioplegia	6	-83 ± 1 mV ³	-49.5 ± 1 mV ^{2, 4}	Kleber AG (1983) Circ Res. <u>52</u> (4) 442-50

¹ Adenosine (200 uM) and lidocaine (500 uM) was in 10 mM glucose-containing Krebs-Henseleit solution pH 7.4

² Measured using 3M KCl microelectrodes

³ Membrane potential was calculated from the Nernstian distribution of K⁺ ion between intra- and extra-cellular compartments of left ventricle as described in Masuda, Dobson and Veech (1990) The Donnan Near-Equilibrium system of heart. J. Biol. Chem 265 (33) 20321-34

⁴ isolated perfused guinea pig heart.

⁵ Healthy (non-injured) pre-arrest perfused isolated rat hearts in the working mode

Table 16:

2 hour Arrest Protocol	Treatment	n	Heart Rate (bpm)	Aortic Flow (ml/min)	Coronary Flow (ml/min)	Rate Pressure Product (mmHg/min)	O ₂ Consumption (μmol/min/g dry weight)®
5 min Pre-Arrest	AL	7	259 ± 20	33.2 ± 2.7	17.1 ± 1.8	30998 ± 2046	45.3 ± 4.30
	St.T	8	259 ± 13	34.5 ± 2.1	18.0 ± 1.3	31329 ± 1720	46.1 ± 2.60
15 min Recovery	AL	7	215 ± 24	17.0 ± 3.6	15.3 ± 1.4	24934 ± 2506	53.6 ± 7.2
	St.T	8	108 ± 32*	5.9 ± 3.8	7.3 ± 2.9*	9514 ± 3737*	16.4 ± 6.6
30 min Recovery	AL	7	248 ± 22	25.5 ± 2.3	15.4 ± 1.6	28722 ± 2149	51.6 ± 5.6
	St.T	8	148 ± 47*	9.4 ± 7.0*	8.93 ± 4.6	12498 ± 6863*	18.9 ± 7.5
60 min Recovery	AL	7	245 ± 26	24.6 ± 2.7	13.8 ± 1.7	27958 ± 2457	49.8 ± 6.5
	St.T	8	147 ± 45*	7.7 ± 5.9*	8.35 ± 4.4	11808 ± 6533*	18.8 ± 7.8

* denotes significance between treatment groups' p<0.05 ** denotes significance between treatment groups p<0.001
 ®To convert from μmol/min/g dry weight to wet weight divide by 7.46 for both pre-arrest groups, and by 9.26 (AL hearts) and 7.41 (St. Thomas' hearts) in recovery

Figure 34

Table 17:

4 hour Arrest Protocol	Treatment	n	Heart Rate (bpm)	Aortic Flow (ml/min)	Coronary Flow (ml/min)	Rate Pressure Product (mmHg/min)	O ₂ Consumption (μmol/min/g dry weight) [®]
5 min Pre-Arrest	AL	9	275 ± 13	36.5 ± 1.7	16.28 ± 1.0	32338 ± 1084	50.3 ± 3.4
	St.T	7	259 ± 13	41.2 ± 4.2	16.03 ± 1.3	31508 ± 1672	57.2 ± 1.8
15 min Recovery	AL	9	229 ± 16	19.8 ± 3.6	13.9 ± 1.5	25327 ± 1555	55.0 ± 6.4
	St.T	7	67 ± 28**	2.7*	2.3**	3815 ± 3040**	5.7 ± 5.1**
30 min Recovery	AL	9	239 ± 19	24.6 ± 2.9	11.5 ± 1.0	26684 ± 1669	45.7 ± 4.1
	St.T	7	79 ± 26**	2.4**	2.9*	4137 ± 3170 **	6.1 ± 5.5**
60 min Recovery	AL	9	249 ± 17	25.6 ± 3.3	11.4 ± 1.3	27569 ± 1577	44.6 ± 4.8
	St.T	7	83 ± 30**	2.1**	2.6*	4359 ± 3527**	7.1 ± 6.5**

* denotes significance between treatment groups $p < 0.05$ ** denotes significance between treatment groups $p < 0.001$

Only 1 of 7 St Thomas' hearts had measurable aortic and coronary flows and only the mean values are presented.

® To convert from μmol/min/g dry weight to wet weight divide by 7.46 for both pre-arrest groups, and by 9.26 (AL hearts) and 7.41 (St. Thomas' hearts) in recovery

Figure 35